WHAT IS CLAIMED IS:

1. A non-painful composition of a hydrophobic protein suitable for injection in a human comprising:

(a) a hydrophobic protein;

(b) an amount of a zwitterionic detergent that is less than the amount required to solubilize the protein; and

(c) an amount of a pharmaceutically acceptable nonionic detergent effective to maintain solubility of the protein in a pharmaceutically acceptable carrier.

2. The composition of claim 1, wherein the zwitterionic detergent is selected from the group consisting of *n*-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-(N,N-*n*-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-[(3-Cholamidopropyl) dimethylammonio]-1-propanesulfonate; 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate; and *n*-Dodecyl-N,N-dimethylglycine.

3. The composition of claim 2, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate.

4. The composition of claim 1, wherein the nonionic detergent is selected from the group consisting of alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl), Polyoxyethylene (20) sorbitan monolaurate, Polyoxyethylene (20) sorbitan monooleate and Polyoxyethylene (35) Lauryl Ether.

5. The composition of claim 4, wherein the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl).

6. The composition of claim 1, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate in a final concentration that

is below its critical micelle concentration (CMC) and the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl) in a final concentration that is above its CMC.

7. The composition of claim 1, wherein the hydrophobic protein is an integral membrane protein.

8. The composition of claim 7, wherein the integral membrane protein is derived from an infectious agent selected from the group consisting of a bacterium, a virus, a parasite and a prion.

9. The composition of claim 8, wherein the infectious agent is a bacterium.

10. The composition of claim 9, wherein the integral membrane protein is a porin.

11. The composition of claim 9, wherein the integral membrane protein is a gonococcal porin.

12. The composition of claim 9, wherein the integral membrane protein is a Meningococcal porin.

13. A method of immunizing a human, which method comprises parenterally administering the composition of claim 8, wherein the infectious agent is a human pathogen.

14. A method for producing a less-painful immunogenic composition of a hydrophobic protein in a pharmaceutically acceptable carrier suitable for administering to a mammal, comprising the steps of

(a) solubilizing said hydrophobic protein with a zwitterionic detergent to make a first composition;

(b) altering said first composition, such that the altered composition is less painful as compared to said first composition.

15. The method of claim 14, wherein the altering step (b) is selected from the group consisting of (i) diluting the zwitterionic detergent, (ii) exchanging the zwitterionic detergent with a non-pain causing nonionic detergent, and (iii) adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.

16. The method of claim 15, wherein the altering step (b) is diluting the zwitterionic detergent with a non-pain causing nonionic detergent.

17. The method of claim 15, wherein the altering step (b) is exchanging the zwitterionic detergent with a non-pain causing nonionic detergent.

18. The method of claim 15, wherein the altering step (b) is adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.

19. The method of any of claims 16, 17 or 18, wherein the zwitterionic detergent is selected from the group consisting of *n*-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-(N,N-*n*-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-[(3-Cholamidopropyl) dimethylammonio]-1-propanesulfonate; 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate; and *n*-Dodecyl-N,N-dimethylglycine.

20. The method of any of claims 16, 17 or 18, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate.

21. The method of any of claims 16, 17 or 18, wherein the nonionic detergent is selected from the group consisting of alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl), Polyoxyethylene (20) sorbitan monolaurate, Polyoxyethylene (20) sorbitan monooleate and Polyoxyethylene (35) Lauryl Ether.

22. The method of any of claims 16, 17 or 18, wherein the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl).

23. The method of any of claims 16, 17 or 18, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate in a final concentration that is below its CMC and the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl) in a final concentration that is above its CMC.

24. The method of claim 14, wherein the altering step (b) is diluting said zwitterionic detergent and wherein the hydrophobic protein is in a precipitated form.

25. The method of any of claims 16, 17 or 18, wherein the hydrophobic protein is an integral membrane protein derived from an infectious agent selected from the group consisting of a bacterium, a virus, a parasite and a prion.

26. The method of any of claims 16, 17 or 18, wherein the infectious agent is a bacterium.

27. The method of any of claims 16, 17 or 18, wherein the integral membrane protein is a porin.

28. The method of any of claims 16, 17 or 18, wherein the zwitterionic detergent is diluted to below the critical micelle concentration.

29. The method of any of claims 16, 17 or 18, wherein the integral membrane protein is a gonococcal porin.

30. The method of any of claims 16, 17 or 18, wherein the integral membrane protein is a Meningococcal porin.

31. The method of any of claims 16, 17 or 18, wherein the pain is reduced by at least about 50% as measured in the rat footpad model.

32. A method of reducing the pain associated with administering an immunogenic composition comprising a hydrophobic protein and a zwitterionic detergent into a mammal, which method comprises

(a) altering said composition, such that the altered composition is less painful as compared to the unaltered composition, and

(b) administering said immunogenic composition.

33. The method of claim 32, wherein the altering step (a) is selected from the group consisting of (i) diluting said zwitterionic detergent, (ii) exchanging said zwitterionic detergent with a non-pain causing nonionic detergent, and (iii) adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.

34. The method of claim 33, wherein the altering step (a) is diluting said zwitterionic detergent with a non-pain causing nonionic detergent.

35. The method of claim 33, wherein the altering step (a) is exchanging said zwitterionic detergent with a non-pain causing nonionic detergent.

36. The method of claim 33, wherein the altering step (a) is adding a non-pain causing nonionic detergent but keeping the concentration of said zwitterionic detergent constant.

37. The method of any of claims 34, 35, and 36, wherein said zwitterionic detergent is selected from the group consisting of *n*-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-(N,N-*n*-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-[(3-Cholamidopropyl) dimethylammonio]-1-propanesulfonate; 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate; and *n*-Dodecyl-N,N-dimethylglycine.

38. The method of any of claims 34, 35, and 36, wherein said zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate.

39. The method of any of claims 34, 35, and 36, wherein the nonionic detergent is selected from the group consisting of alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl), Polyoxyethylene (20) sorbitan monolaurate, Polyoxyethylene (20) sorbitan monooleate and Polyoxyethylene (35) Lauryl Ether.

40. The method of any of claims 34, 35, and 36, wherein the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl).

41. The method of any of claims 34, 35, and 36, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate in a final concentration that is below its CMC and the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl) in a final concentration that is above its CMC.

42. The method of any of claims 34, 35, and 36, wherein the hydrophobic protein is an integral membrane protein.

43. The method of any of claims 34, 35, and 36, wherein the integral membrane protein is derived from an infectious agent selected from the group consisting of a bacterium, a virus, a parasite and a prion.

44. The method of any of claims 34, 35, and 36, wherein the infectious agent is a bacterium.

45. The method of any of claims 34, 35, and 36, wherein the integral membrane protein is a porin.

46. The method of any of claims 34, 35, and 36, wherein the integral membrane protein is a gonococcal porin.

47. The method of any of claims 34, 35, and 36, wherein the integral membrane protein is a Meningococcal porin.

48. The method of any of claims 34, 35, and 36, wherein the solubility of the hydrophobic protein is maintained in said nonionic detergent.

49. The method of claim 33, wherein the altering step (a) is diluting said zwitterionic detergent and wherein the hydrophobic protein is in a precipitated form.

50. The method of any of claims 34, 35, and 36, wherein the pain is measured in the rat footpad model.

51. The method of claim 50, wherein the altered composition produces at least about a 50% reduction in pain as measured in the rat footpad model as compared to the unaltered composition.

52. A method of reducing the pain associated with administering an immunogenic composition comprising a hydrophobic protein and a zwitterionic detergent into a mammal, which method comprises

(a) altering said composition, such that the altered composition produces a reduction in pain as measured in the rat footpad model as compared to the unaltered composition, and

(b) administering said immunogenic composition

wherein the altered composition produces at least about a 50% reduction in pain as measured in the rat footpad model as compared to the unaltered composition.

53. The method of claim 52, wherein the altering step (a) is selected from the group consisting of (i) diluting said zwitterionic detergent with a non-pain causing nonionic detergent, (ii) exchanging the zwitterionic detergent with a non-pain causing nonionic detergent, and (iii) adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.

54. The method of claim 53, wherein the altering step (a) is diluting the zwitterionic detergent with a non-pain causing nonionic detergent.

55. The method of claim 53, wherein the altering step (a) is exchanging the zwitterionic detergent with a non-pain causing nonionic detergent.

56. The method of claim 53, wherein the altering step (a) is adding a non-pain causing nonionic detergent but keeping the concentration of the zwitterionic detergent constant.

57. The method of any of claims 54, 55, and 56, wherein the zwitterionic detergent is selected from the group consisting of *n*-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-(N,N-*n*-Hexadecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate; 3-[(3-Cholamidopropyl) dimethylammonio]-1-propanesulfonate; 3-[(3-Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate; and *n*-Dodecyl-N,N-dimethylglycine.

58. The method of any of claims 54, 55, and 56, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate.

59. The method of any of claims 54, 55, and 56, wherein the nonionic detergent is selected from the group consisting of alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl), Polyoxyethylene (20) sorbitan monolaurate, Polyoxyethylene (20) sorbitan monooleate and Polyoxyethylene (35) Lauryl Ether.

60. The method of any of claims 54, 55, and 56, wherein the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl).

61. The method of any of claims 54, 55, and 56, wherein the zwitterionic detergent is *n*-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate in a final concentration that is below its CMC and the nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl) in a final concentration that is above its CMC.

62. The method of any of claims 54, 55, and 56, wherein the hydrophobic protein is an integral membrane protein.

63. The method of any of claims 54, 55, and 56, wherein the integral membrane protein is derived from an infectious agent selected from the group consisting of a bacterium, a virus, a parasite and a prion.

64. A method of maintaining solubility of a hydrophobic protein in an immunogenic composition, which method comprises:

solubilizing a hydrophobic protein in a non-pain causing nonionic detergent, wherein non-pain causing nonionic detergent is alpha-[4-(1,1,3,3-tetramethylbutyl)phenyl]-omega-hydroxypoly(oxy-1,2-ethanediyl).

65. A method for immunizing humans with compositions containing hydrophobic membrane proteins without causing pain, which method comprises selecting Triton X-100 as a pharmaceutically acceptable detergent for maintaining solubility of hydrophobic proteins in the final formulation; wherein the concentration of Triton X-100 is above the CMC.